

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	McDonald et al.	Examiner:	OLSON, Eric
Serial No:	10/613,788	Art Unit:	1623
Filed:	July 3, 2003	Attorney	
		Ref. No:	8105-009-US-CON
Title: METHOD OF LONG TERM TREATMENT OF GRAFT-VERSUS-HOST DISEASE USING TOPICAL ACTIVE CORTICOSTEROIDS			

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.132

Dear Sir:

I, George B. McDonald, M.D., hereby make the following
declaration:

1. I received my medical degree (M.D.) from
Washington University in St. Louis, MO., in 1967, completed

my residency in internal medicine at the University of Washington Affiliated Hospitals in Seattle, Washington, in 1969; and completed my fellowship in Gastroenterology at the University of Washington in Seattle, Washington in 1975. I have been on the faculty in the Department of Medicine at the University of Washington, Seattle, Washington, since 1975, and I am currently a Professor in the Department of Medicine. I have been affiliated with the Fred Hutchinson Cancer Research Center since 1975, and have been the Head of the Gastroenterology/Hepatology Section and a Member there since 1988. I spent a sabbatical year of research in the field of inflammatory bowel disease at Oxford University (U.K.) during 1983-1984. My primary research interests, for which I have been continuously funded by the National Institutes of Health for over 25 years, are in the complications of hematopoietic cell transplant, including graft-vs.-host disease. I have published over 200 original papers, reviews, and book chapters and have presented over 150 scientific papers at national meetings.

2. In 1998, I licensed my utility patent on prevention of acute GVHD with oral beclomethasone dipropionate (U.S. Patent No. 6,096,731) and my declaration of Orphan Drug Status for oral beclomethasone dipropionate for the indication acute GVHD from the U.S. Food and Drug Administration to Enteron Pharmaceuticals, Inc. I became a consultant to Enteron Pharmaceuticals at this time, and remain so. Enteron Pharmaceuticals, Inc. was later acquired by DOR BioPharma.

3. I was the principal investigator of the study cited by the Examiner as prior art presently of record ("McDonald et al").

4. At the time of the filing of this application, it was well known within the field of corticosteroid therapeutics that there was considerable risk to patients receiving long term glucocorticoid administration. The risks were known to be the following: immunosuppression leading to fatal and non-fatal infections; diabetes; hypertension; bone loss and fractures; muscle weakness and debility; Cushingoid appearance; neuropsychiatric disturbances; and suppression of the hypothalamic-pituitary-adrenal axis leading to Addison's disease (hypofunction of the adrenal gland).

5. At the time of the filing of this application, one skilled in the art would consider administration of beclomethasone dipropionate beyond 30 days as long term glucocorticoid administration.

6. In McDonald et al., one of the main reasons for ceasing treatment at 29 days was due to the potential for the occurrence of the above mentioned risks associated with long term glucocorticoid administration. In a previous publication describing a phase I trial of oral beclomethasone dipropionate for acute GVHD, I had demonstrated a statistically significant reduction in indices of adrenal gland function after 28 days of oral beclomethasone dipropionate therapy. It was not known whether extending treatment with oral beclomethasone dipropionate beyond this time period was safe.

7. It is my opinion that there would be no motivation of one skilled in the art at the time of the filing of the present application to extend administration of beclomethasone dipropionate beyond 30 days, without evidence that this therapy was safe and effective. To do so would inherently carry the above identified risks.

8. I declare that all statement made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Respectfully submitted,

This 23rd day of March, 2007


George B. McDonald, M.D.